REMARKS

Reconsideration and allowance of the present application is respectfully requested in view of the foregoing amendments and the following additional remarks which have addressed all the issues raised in the March 26, 2007, Office Action or otherwise have rendered them moot.

Claims 36, 38, 41, 42, 44, and 67 stand rejected under 35 U.S.C. § 103 (a) as allegedly obvious over Itay (U.S. 5, 053, 050), in view of Mikos (1996 US Patent 5,522,895; reference A), Rosenthal et al. (1995, U.S. Patent 5, 466, 462, reference B), and Jakob et al. (WO 99/21497; and German-to-English translation).

Claim 37 is rejected under 35 U.S.C. § 103 (a) as allegedly obvious over Itay (U.S. 5, 053, 050), Mikos, Rosenthal et al., and Jakob et al. as applied to claims 36, 38, 41, 42, 44, and 67 above, and further in view of Goldstein et al. (1999, U.S. Patent 5,962,427: reference C) and Vacanti et al. (1998, U.S. Patent 5,804,178; reference D).

Claims 39 and 43 are rejected under 35 U.S.C. § 103 (a) as allegedly obvious over Itay (U.S. 5, 053, 050), Mikos, Rosenthal et al., and Jakob et al. as applied to claims 36, 38, 41, 42, 44, and 67 above, and further in view of Wevers (1981, U.S. Patent 4,246,660) and Dunn et al. (1995, Journal of Biomedical Materials Research 29:1363-1371).

Applicants gratefully acknowledge telephonic Interview with the Examiner on May 14, 2007. The foregoing amendments and the following remarks have taken into account the outcome of that interview.

Rejections under 35 U.S.C. § 103(a)

Claims 36, 38, 41, 42, 44, and 67 stand rejected under 35 U.S.C. § 103 (a) as allegedly obvious over Itay (U.S. 5, 053, 050), in view of Mikos (1996 US Patent 5,522,895; reference A), Rosenthal et al. (1995, U.S. Patent 5, 466, 462, reference B), and Jakob et al. (WO 99/21497; and German-to-English translation).

The Examiner admits that Itay does not teach an *in vitro* composition comprising both cultured cartilage cells and cultured bone cells, said composition comprising cartilage cells on one face thereof and bone cells on the opposing face. The Examiner asserts, however, that Mikos teaches seeding osteoblasts in growth medium onto a biodegradable polymer, allowing

the suspension to wick into the polymer foam, and culturing the cells on the polymer to allow them to attach to the foam.

The Examiner further asserts that Rosenthal *et al.* teach that fibrin and polyglycolic acid are functional equivalents in the tissue engineering and wound healing arts.

The Examiner further asserts that Jakob *et al.* teach a composition comprising both a bone side and a cartilage side; the composition of Jakob et al. being a column of tissue that has been removed from a donor site at the articular face of a bone. The Examiner further asserts that Jakob et al. also teach a composition comprising cartilage cells cultured *in vitro* on bone-replacement material.

The Examiner concludes that it would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the *in vitro* bone construct of Mikos and the *in vitro* cartilage construct of Itay to yield a composition comprising cultured cartilage on one side and cultured bone on the opposite side because Jakob *et al.* teach that compositions so configured may be implanted into the articular portions of bones to effectively treat defects. Applicants respectfully disagree and now traverse as follows.

Applicants strongly disagree with the propriety of the combination asserted above by the Examiner. The Examiner is arguing that natural tissue grafting as taught by Jakob et. al., obviates as uninventive, any attempt to generate biocompatible tissue or organ *in vitro* merely because the cells that could form part of that *in vitro* tissue or organ have been separately cultured at some point by another. In that sense, why should inventors labor in the field of tissue engineering only for the Examiner to point out that the natural tissue has vitiated their efforts, whereas the main object of such endeavor is to attempt to generate artificial tissue *in vitro*? Naturally the functionality and structure of the natural tissue motivates such endeavor, but that is not the relevant inquiry for patentability purposes; the inquiry is whether a functional joint can be generated *in vitro* and not whether the resulting product looks like the real thing. It is to Applicants' inventive credit, not to their discredit, that their artificial joint mimics Jakob's *et al.*'s natural bone graft. Applicants believe that there were not only the first to do so, but the difficulties in culturing animal cells in the laboratory make the ability to construct a biological joint wholly *in vitro* a highly inventive undertaking.

If the artificial joint looks like the real thing, it is the very inventive genius which Applicants are seeking protection for. After all, it is one of the objects of the instant invention to

generate joint-mimetic construct *in vitro* and the ultimate object is to engineer one as close in structure and function to a natural joint as possible. Thus, the relevant inquiry is whether Jakob *et al.* and other cited references in anyway teach, suggest, motivate, or else point to the likelihood of success of an attempt to engineer a functional biological joint *in vitro.*

Nor do the Applicants contend that they are the first to culture bone cells or cartilage cells. Nor do the Applicants suggest that they are the first to realize that animal cells in general are anchorage dependent. Applicants contend, however, that they are the first to culture anchorage dependent osseous and cartilaginous cells suitably anchored on biocompatible materials and arranged in such a manner as to constitute a novel and unobvious joint construct.

As now amended, Applicants' *in vitro* joint construct comprise a joint side, an anchor side, and an interlocking zone for effecting an *in vitro* integration of both sides in order to *in vitro* create the functional equivalent of a joint. Support for the interlocking zone may be found in the last paragraph of pages 5 and 11; and Figures 1f and 1g.

Thus, although Applicants believe that anchorage-dependent cartilage and osseous cells may have been grown by others before the date of this invention, Applicants do not believe that a natural organ or tissue being composed of cells provide motivation to preclude the inventiveness of a wholly *in vitro* joint construct aimed at generating in the laboratory, an organ or tissue as close to the natural organ as possible. And even if it were so, the in vitro construct of the instant invention differs in material structural respects from the natural joint. For one thing, the interlocking zone mentioned above is a non-natural feature; for another thing, the nerves, gross histological components, connective tissues, and vascularization of a natural joint are lacking in the artificial joint of the present invention, and whereas the artificial joint of the present invention can be used to effect repair of damaged bone, it is nevertheless a man-made joint and should be regarded as such for patentability purposes.

Nor do the Applicants believe that their interlocking bone-cartilage articulating junction approximate its anatomical counterpart. And neither can it reasonably be said that the asserted prior art obviated the inventiveness of finding a way, in vitro, to integrally connect the cartilage side and the osseous side in order to engineer an orthopaedically functional joint construct.

On the basis of the foregoing, Applicants assert that there is no basis to maintain the obviousness rejection of the instant invention and it is respectfully requested that it be withdrawn.

Claim 37 is rejected under 35 U.S.C. § 103 (a) as allegedly obvious over Itay (U.S. 5, 053, 050), Mikos, Rosenthal et al., and Jakob et al. as applied to claims 36, 38, 41, 42, 44, and 67 above, and further in view of Goldstein et al. (1999, U.S. Patent 5,962,427: reference C) and Vacanti et al. (1998, U.S. Patent 5,804,178; reference D). Further, claims 39 and 43 are rejected under 35 U.S.C. § 103 (a) as allegedly obvious over Itay (U.S. 5, 053, 050), Mikos, Rosenthal et al., and Jakob et al. as applied to claims 36, 38, 41, 42, 44, and 67 above, and further in view of Wevers (1981, U.S. Patent 4,246,660) and Dunn et al. (1995, Journal of Biomedical Materials Research 29:1363-1371).

Claim 37, 39 and 43, being dependent on claim 36, it is respectfully asserted that the foregoing have adequately addressed this ground for rejection or rendered it moot.

Suffice it to state that the genius of an invention is often a combination of known elements that in hindsight seem preordained. It is improper to use the inventor's patent as an instruction book on how to reconstruct the prior art. Panduit Corp. v. Dennison Mfg. Co., 810 F.2d 1561, 1 USPQ2d 1593 (Fed. Cir. 1987). The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that the process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art. Both the suggestion and the expectation of success must be founded in the prior art, not in the Applicant's disclosure. *In re O'Farrell*, 853 F.2d 894, 7 USPQ2d 1673 (Fed. Cir. 1988).

Applicants respectfully ask that the Examiner to not let hindsight hamper the elegance of the instant wholly-engineered joint construct, if in retrospect, it appears simple enough to the Examiner. Many a Scientists know and appreciate the difficulties of culturing a monolayer of anchorage dependent animal cells of a particular kind, let alone co-culturing animal cells of more than one kind, let alone doing so in a three-dimensional construct, let alone doing so with a structural articulation as complex as a joint. If this invention were obvious, many would have done it because there is a huge orthopedic need for constructs that would accelerate joint healing without the need to graft orthopedic material taken from a different part of the patient's anatomy. Again, the mere fact that Scientists have grown cells used in the instant invention in the past does not in anyway render obvious the engineering of an organ or tissue comprising those cells.

The Examiner is respectfully asked to reconsider and withdraw these grounds for rejection particularly for the fact that even if the Examiner insists on making these combinations, the combined art still does not anticipate the invention of claim 36. Particularly, the in vitro integration of the joint and the anchor side of the joint construct renders the resulting artificial construct different from any combination which the prior art would teach. As such, it is again respectfully requested that this ground for rejection be withdrawn.

CONCLUSION

All of the stated grounds for rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn and the claims allowed to issue. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

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